

IT IS CLAIMED:

1. A method of treating a systemic infection which is localized at a site other than the fixed macrophages
5 residing in the liver or the spleen, comprising

administering to the subject, by parenteral injection, a composition of liposomes (i) composed of vesicle-forming lipids including an amphipathic vesicle-forming lipid derivatized with a hydrophilic biocompatible polymer of a
10 size and in a molar amount effective to extend liposome blood circulation time, measured 24 hours after said injection, severalfold and over that achievable in the absence of the hydrophilic polymer (ii) having a selected mean particle diameter in the size range between about
15 0.07-0.20 microns, and (iii) containing in liposome-entrapped form, a therapeutic compound effective against the source of the infection, and

by said injecting, concentrating the liposomes in the infected tissue, thereby to concentrate liposome-entrapped
20 compound at the site of infection.

2. The method of claim 1, wherein the hydrophilic biocompatible polymer is a polyethylene glycol having a molecular weight between about 300 and 5,000 daltons.
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3. The method of claim 1, wherein the hydrophilic biocompatible polymer is selected from the group consisting of polyglycolic acid (PGA), polylactic acid (PLA), a copolymer of PGA and PLA, and polyvinyl alcohol.
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4. The method of claim 1, wherein the infection is bacterial in origin and the therapeutic compound is an antibiotic.

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5. The method of claim 4, wherein at least about 60% of the antibiotic agent is in liposome-entrapped form.

6. The method of claim 1, wherein the antibiotic agent is an aminoglycoside antibiotic, the concentration of which entrapped in the liposomes is greater than 20 μg compound/ μmole liposome lipid.

7. The method of claim 1, wherein the infection site is lung, the source of the infection is Klebsiella, and the therapeutic agent is gentamicin.

8. For use in a method of treating a site of systemic infection which is localized at a tissue site other than the fixed macrophages residing in the liver or the spleen, an injectable liposome composition characterized by:

(a) composed of vesicle-forming lipids including an amphipathic vesicle-forming lipid derivatized with a hydrophilic biocompatible polymer of a size and in a molar amount effective to extend liposome blood circulation time, measured 24 hours after said injection, severalfold and over that achievable in the absence of the hydrophilic polymer,

(b) liposomes having a selected mean particle diameter in the size range between about 0.07-0.20 microns,

(c) containing in liposome-entrapped form, a therapeutic compound active against the pathogen causing the infection,

(d) ability to accumulate selectively in the infected tissue following parenteral administration, thereby to concentrate liposome-entrapped drug at the infection site.

9. The composition of claim 8, wherein the hydrophilic polymer is a polyethyleneglycol having a molecular weight between about 300-5,000 daltons.

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10 11. The composition of claim ¹⁰9, wherein the hydrophilic polymer is selected from the group consisting of polyglycolic acid (PGA), polylactic acid (PLA), a copolymer
5 of PGA and PLA, and polyvinyl alcohol.

11 12. The composition of claim ¹¹9, for use in treating such an infected region wherein the therapeutic compound is an aminoglycoside antibiotic, and the concentration of
10 compound entrapped in the liposomes is greater than about 20 μg compound/ μmole liposome lipid.

13 13. The composition of claim ¹²9, wherein the site of infection is the lung, and the aminoglycoside antibiotic is
15 gentamicin.

14. A method of preparing an antimicrobial agent for localization in an infected region of tissue, when the agent is administered by parenteral injection, comprising
20 entrapping the agent in liposomes which are characterized by:

(a) composed of vesicle-forming lipids including an amphipathic vesicle-forming lipid derivatized with a hydrophilic biocompatible polymer of a size and in a molar
25 amount effective to extend liposome blood circulation time, measured 24 hours after said injection, severalfold and over that achievable in the absence of the hydrophilic polymer,

(b) liposomes having a selected mean particle diameter in the size range between about 0.07-0.20 microns,
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(c) containing in liposome-entrapped form, a therapeutic compound effective against the source of the infection.

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(d) ability to accumulate selectively in the infected tissue following parenteral administration, thereby to concentrate liposome-entrapped drug at the infection site.

5 10 ¹⁴ 15. The method of claim ¹³ 14, wherein the agent is an aminoglycoside antibiotic drug.

15 16. The method of claim ¹⁴ 15, wherein the aminoglycoside is gentamicin.

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